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Abstract: PURPOSE OF REVIEW To review the developments within paediatric anaesthesia and describe the various factors that have contributed to the improvements in anaesthesia-related outcomes in children. RECENT FINDINGS During the years substantial improvements in paediatric anaesthesia-related outcomes has derived from safety advances in equipment, drugs, human factor analysis, professional standardization and organization, subspecialty care and regionalization. However, universally agreed outcome measures are lacking. SUMMARY Despite a steadily and significant improvement in paediatric anaesthesia-related outcomes over the years further and future improvements are still necessary in areas such as adverse-event reporting and long-term neurocognitive outcomes with much more focus on patient/family-centred outcomes. Clinical experts and stakeholders should meet and agree on a consensus to identify indicators that could act as outcome measures in future large-scale prospective observational studies and clinical trials. Such an approach will foster benchmarking and continuous quality assessment and improvement at individual, institutional, interinstitutional, regional, national and international levels and facilitate larger scale clinical research. Furthermore, it will attain a high public health importance and will facilitate comparisons between healthcare provision models leading to optimization of perioperative care delivery.

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Keywords
anaesthesia, children, outcome, safety and quality, surgery

INTRODUCTION

The field of anaesthesia is often cited as a model for patient safety initiatives [1▪] and as a specialty has benefitted tremendously from introducing fundamental principles of safety science. Avoidance of morbidity and mortality is viewed as a basic human right and the overwhelming expectation by patients and parents is complete recovery and patient safety. Significant improvements in frequent but non-life threatening anaesthesia-associated and surgery-associated problems, for example undertreated pain, postoperative nausea and vomiting (PONV) and postoperative behavioural problems have resulted in high level of satisfaction following day surgical procedures. The focus in paediatric anaesthesia practice, as in other paediatric subspecialties, has shifted from patient-specific to large national or international cohort outcomes as refinements in perioperative care are no longer quantifiable. In other words, the previously most basic and most commonly outcome measure, survival, has become a nearly unmeasurable discriminator of quality. A relatively small volume of patients per institution, an increasing breadth of paediatric coexisting conditions, diversified surgical procedures, and even the paediatric physician's focus on individual outcomes have contributed to a delay of exploring of other relevant paediatric surgical and anaesthesia outcomes on a large scale. This has been greatly facilitated by research and quality improvements of neuro-developmental safety in children over the past 20 years

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KEY POINTS

- Outcome following anaesthesia in children has improved dramatically over the years.
- Given the extremely low incidence of cardiac arrest, this outcome has become a poor descriptor of the quality of anaesthesia care in children. Once the incidence of critical and severe complications has been minimized other factors related to organizational and system performance, professionalism, comfort and child-centricity may become increasingly important.
- At the present time there is no consensus on which outcomes are a priority following paediatric anaesthesia. Clinical experts and stakeholders should meet and agree on a consensus to identify indicators that could act as outcome measures in future observational studies and clinical trials.
- Prospective large multicenter databases of perioperative electronical data and these preidentified indicators should be established. These will foster benchmarking and continuous quality assessment and improvement at individual, institutional, interinstitutional, regional, national and international levels and facilitate larger scale clinical research.

highlighted numerous factors that are relevant to patients, parents and professionals [2▪,3▪,4,5▪,6▪▪].

There is no benefit to focus on matters that are nonmodifiable (i.e. the need to provide anaesthesia and pain control as well as nonmodifiable comorbidity) when considering outcomes after anaesthesia and surgery in children. Instead, attention should be directed towards development of an understanding of what outcomes can be influenced by perioperative care and at the same time matters to all stakeholders [7].

The article will, therefore, review the development of outcome measurements and improvement practices in perioperative paediatric anaesthesia care with the goal to provide background knowledge to assist interpretation of emerging quality and safety measures and initiatives in this specialty.

HISTORICAL PERSPECTIVES

The first outcome of anaesthesia was efficacy: surgery could be performed more reliably on more patients particularly when they lie still without pain or awareness. The first ether anaesthetic was administered by Crawford Long in 1842 in Pennsylvania and the first paediatric inhalational anaesthetic induction was reported in 1847 [2▪]. It became immediately apparent that the administration of general anaesthesia was not without side effects and complications. The issue of mortality was readily identified, particularly in relation to a full stomach. For many years it was debated whether ether or chloroform was the safest anaesthetic available, mainly based on case reports or small case-series.

Apparently the first robust analysis into anaesthesia of safety came from India in 1889–1890. Lt-Col Edward Lawrie reported on his own experience with chloroform anaesthesia and a surprisingly low incidence of perioperative death of one in 17 300 anaesthetics [8]. In addition to this, he also reported on several 'best practice' principles, some of these are still considered important by today's standards. Some of these principles are: proper patient selection, the positioning of patients to ensure patency of airway, the use of respiration details for depth of anaesthesia and the use of premedication to reduce anxiety.

More modern reports of anaesthesia-related morbidity and mortality originate from 1954 comprising almost 600 000 anaesthetics from 10 university hospitals reporting an anaesthesia-related mortality rate of one in 1560 cases [9▪▪]. Certain drugs (curare, suxamethonium and volatiles) were identified as 'troublesome' and system-related issues such as inadequate training or lack of supervision were also recognized. Unsurprisingly, the high mortality rate made 'death under anaesthesia' a public health concern.

The subsequent years were characterized by a significant increase in knowledge of biology, physiology, pharmacology and technology making modern anaesthesia safer. Both technical and nontechnical skills were recognized as fundamental to the safe provision of perioperative care. As a result, today's anaesthesia-related mortality in children is extremely low in developed countries, making this outcome measure a poor single descriptor of the quality of anaesthesia care in children.

Minimal standards for anaesthesia and patient monitoring had perhaps the biggest impact on the reduction of perioperative mortality and were suggested almost simultaneously by the Harvard Medical School Department of Anaesthesia [10▪] and the American Society for Anesthesiologist more than 30 years ago (www.asahq.org/publicationsAndServices/standards/02.pdf). These included but were not limited to: pulse-oximeter, ECG, noninvasive blood pressure (BP), temperature, end-tidal CO_2 and FiO_2 measurements as well as the use of alarms for low oxygen concentration, ventilator disconnection and most importantly the continuous presence of a trained anaesthesia care provider. They represent the accepted minimal standard for monitoring and conduct of anaesthesia and have provided a template for anaesthesia documentation ever since thus

serving a crucial role in preventing hypoxic-ischaemic injury. These standards were not based on evidence from clinical trials but rather from the analysis of critical incidents and applying knowledge of pathophysiology, human factors and technology. They are now (almost) universally adopted worldwide.

CARDIAC ARRESTS AND CRITICAL EVENS IN PAEDIATRIC ANAESTHESIA

Cardiac arrest is the mostly feared and not uncommon complication during and following anaesthesia and surgery in children [11]. The two most cited studies on this matter are derived from the Pediatric Perioperative Cardiac Arrest (POCA) Registry [12,13], In the POCA I study (1994–1997) describing 289 perioperative cardiac arrests, 52% were anaesthesia-related. In the POCA II study (1998–2004) describing 397 perioperative cardiac arrests, 49% were anaesthesia-related. Significantly, patient-characteristics and causes between the two studies were compared in a separate analysis. These included anaesthesia-related cardiac in American society of anesthesiologists physical status classification system (ASA-PS) 1 patients (15 vs. 7%), infants (55 vs. 38%) and emergency cases (21% in both studies). The causes were: cardiovascular (32 vs. 41%), respiratory (20 vs. 27%), drug-related (37 vs. 18%) and equipment-related (7 vs. 5%). Cardiac arrests were commonly preceded by bradycardia, arrhythmias, hypotension, desaturation (and cyanosis) and abnormal end-tidal CO_2. The decline in drug-related cardiac arrests was believed to be due to the switch from halothane to sevoflurane. However, despite these differences the mortality rates were virtually similar (26 vs. 28%). Cardiovascular causes represented a significant proportion in both POCA I and II. In POCA II these were primarily due to hypovolaemia due to sudden blood loss and post-transfusion hyperkalaemia. A recent study could demonstrate that implementation of a specialized paediatric anaesthesia team and training programme was associated with lower incidences of perioperative paediatric cardiac arrests [14▪]. Several other outcome studies on paediatric anaesthesia-related mortality and morbidity have been published over the years [15–17]. An increased risk for significant perioperative complications is recognized in neonates and infants, children with ASA-PS score at least 2, significant associated comorbidities and emergency procedures. Children with anaesthesia-related respiratory events have also an increased risk of severe perioperative complications.

In 2017, the Anaesthesia Practice in Children Observational study reported a significant higher incidence of perioperative severe critical events during paediatric anaesthesia in Europe than previously reported [18▪▪]. Known risk factors such as age, comorbidity and physical status of the child were confirmed and further risk factors identified: Inexperience of the anaesthetic team, age less than 3 years, airway hypersensitivity, snoring and variability across European countries and centres. Respiratory problems during anaesthesia such as laryngospasm and bronchospasm are also more common in children than in adults. Age as a risk factor for adverse respiratory events decreases with 12% per each increasing year of age. Significantly, a multivariate analysis revealed evidence for the beneficial effect of years of experience of the most senior anaesthesia team member for both respiratory and cardiovascular critical events, rather than the type of health institution or providers.

Table 1. Examples of core outcome sets used in anaesthesia

Mortality
Time from injury to surgery
Acute coronary syndrome
Hypotension
Acute kidney injury
Delirium
Pneumonia
Orthogeriatric output
Being out of bed on day 1
Pain

Adepted from [19▪].

OTHER IMMEDIATE AND LATE OUTCOMES

There is a recognized need to further define perioperative outcomes in children similar to adults which may need to be procedure-related [7]. A consensus outcome sets to improve the quality of reporting and facilitate comparisons of studies comparing anaesthesia-related outcomes after hip fracture operations have recently been published (Table 1). Only a few of these are directly applicable in children and there is an increasing need for paediatric anaesthesia societies to agree and collaborate on such standardized outcomes.

Immediate outcomes usually include but are not limited to: Mortality, organ morbidity, pain, PONV, ability to tolerate food and fluids, acute behavioural disturbances and return to normal function. These outcome measures can be found in many perioperative databases, which have been established in many centres worldwide [20▪,21,22]. They provide a measure of the acute performance of local and in some cases national perioperative systems. It is

usually expected that healthy children undergoing minor surgeries should return to normal functions within less than 3 days; however, robust and comparative data on these issues are not available [2▪].

There is also evidence of a substantial longer term (weeks-to-months) behavioural outcome impairment related to paediatric anaesthesia (surgery and hospitalization). These include deterioration in school performance or previously acquired 'normal' bodily functions (micturition), photophobia and nightmares [23–25]. Some of these can be prevented at least partially through preoperative preparation stress-reducing programmes, allowing parental presence during anaesthetic induction and (in selected cases) the use of premedication. A range of longer term organ-system outcomes are emerging in adults with sepsis, trauma, cardiovascular, and abdominal surgery and include incidences and severity of renal insufficiency, acute respiratory distress syndrome, thrombosis, infection, duration of intermittent positive pressure ventilation and length of hospital stay [21,22]. However, similar data are currently unavailable in relation to noncardiac paediatric anaesthesia.

FACTORS THAT MAY AFFECT MEDICAL OUTCOMES

Children undergoing general anaesthesia regularly are at risk to endure hypotension, hypocapnia, hyperglycaemia/hypoglycaemia, dysoxaemia, hypothermia and hyponatraemia with the latter due to inadequate perioperative fluid therapy [26,27▪,28]. Each of these single entities has the potential to affect organ maturation/function and neurocognitive development in addition to serious perioperative cerebral damage, brain death and/or even death. Although there is a general consensus between anaesthesia providers to maintain physiological parameters in the 'normal' or 'safe' range during anaesthesia, we often do not know what these safe values are. For example, the physiological range of BP that allows adequate organ perfusion and oxygen delivery to children during the perioperative period is essentially unknown. Similarly, the systemic BP values leading to cerebral hypoperfusion are also poorly defined [29]. On the other side we clearly know that leaving so far as normal defined BP values during anaesthesia in infants can lead to serious cerebral ischaemic-hypoxic encephalopathy [30]. The complex interaction between cardiac output, hypovolaemia, hypotension, hypo/hyperglycaemia, hypo/hypercapnia in the perioperative setting also remains to be determined for the individual patient. Both preclinical laboratory models and clinical investigations will be necessary to better elucidate these questions and ultimately affect outcomes. Many perioperative complications and clinical details in particular in historical records are not documented or disclosed to parents as long as they remain subclinical. Another major contributing factor affecting outcomes, frequently not considered, is the (in-) experience of anaesthesia care provider and subsequent clinical conduct of anaesthesia in these vulnerable patients [16,31,32]. Competent delivery of perioperative anaesthesia care in a suitably staffed environment may reduce the risk of occurrence of severe perioperative complications [33].

The focus on a safe conduct of anaesthesia has recently been highlighted and emphasis critical elements in perioperative care [27▪]. However, what outcomes if any have priority and should we use to measure the quality of anaesthesia and perioperative care? Subsequent questions necessarily arise: Which outcomes matter most to the children and their families? Which outcomes are most important to clinicians and to clinical researchers? Are these outcomes interrelated? Which outcomes could and should routinely be measured in everyday clinical practice and which ones in clinical trials or guide quality improvement projects [7]?

WHAT SHOULD WE DO?

A commitment to training and education leading to competent high-quality clinical care should lead to better medical and nonmedical outcomes following surgery and anaesthesia. Research into the risks of anaesthetists-related neuromorbidity should be recognized as the principal target in neurodevelopmental research [34]. Instead of focusing on anaesthetic agent effects on the development, we need to primarily define and investigate the interaction of critical elements of safe conduct of anaesthesia (http://www.safetots.org) [27▪]. In addition, the effects of economic pressures on the quality of paediatric anaesthesia care have to be investigated and addressed.

One such approach has recently been developed by the Scientific Workgroup of Paediatric Anaesthetist of the German Society of Anaesthesia and Intensive Care Medicine, focusing on the importance of the quality of anaesthesia conduct and experience of the anaesthetist [35]. Training opportunities need to be revisited and cross-specialty experience and collaboration widened. Higher training in paediatric anaesthesia should include significant experience in neonatology and general paediatric medicine. Formalization and standardization of such fellowships was established in Scandinavia more than 15 years ago (http://www.ssai.info/education/paediatric-anaesthesia) [36]. We also need to recognize that

the operating room environment is important but effectively only a small part of perioperative care requiring paediatricians, critical care physicians, neonatologists and paediatric surgeons to contribute to best care. Regular exchange of clinical experiences and expertise between specialties involved in child health will facilitate a better scientific understanding of the physiology and pharmacology in children. A cross-specialty and cross-institutional approach will facilitate long-term outcome and follow-up studies of changes in clinical practice. The 'art of neonatal anaesthesia' requires and needs a sound scientific base to optimize care for this population. No one single anaesthetic drug or technique will provide a best fit for all situations and anaesthesia providers should both be familiar with general and regional anaesthetic techniques. These should regularly be practiced in the otherwise healthy neonatal population undergoing simple surgeries such as herniotomies, pyloromyotomies and circumcisions. This will help to maintain skills in both general and regional anaesthesia techniques for all neonates. Parents and care providers should be aware of the potential risks of an anaesthetist and institutions not competently trained and updated in neonatal anaesthesia as well as inexperienced with small children. They must be able to ask questions that directly affect perioperative anaesthesia care, such as the availability of a well trained and experienced anaesthesia team, appropriate infrastructure and 24/7 specialist rescue services. All neonates, infants and children have the right for the best perioperative care possible [26,27▪]. The current incidence estimate of one in 200 000 of anaesthesia mortality is so low that comparisons between anaesthesia providers, training programs and centres will require the use of surrogate indicators and subsequent statistical trend analysis. Overinterpretation of lack of differences in outcome data can lead to pressures to reduce quality and cut safety corners for the sake of expediency.

Importantly, parents may be more focused on other issues than those described above. Factors such as courtesy, respect and understanding of the child's needs, trust in nursing quality, feeling that time was taken to address all concerns and comfort in the waiting area and particularly delay of surgical procedure may be more relevant. Thus, factors related to organizational and systems performance, professionalism, comfort and child-centricity may become increasingly important once the incidence of critical and severe complications is minimized [7].

CONCLUSION

At the present time, there is no consensus on which outcomes are a priority following paediatric anaesthesia. Clinical experts and stakeholders should meet and agree on a consensus to identify indicators that could act as outcome measures in future observational studies and clinical trials. Such outcome measures have recently been established in adults and efforts are under way in paediatric populations.

Prospective large multicenter databases of perioperative electronical data and these preidentified indicators should be established. Such a global BigData approach will foster benchmarking and continuous quality assessment and improvement at individual, institutional, interinstitutional, regional, national and international levels and facilitate larger scale clinical research. This approach will attain a high public health importance and will facilitate comparisons between healthcare provision models leading to optimization of perioperative care delivery.

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
- ▪▪ of outstanding interest

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